

April 6, 1952

Dear Rothfels:

One of my students accidentally ran into leucine-inhibition story again, as mentioned in the ms. of your paper to Genetics on the Lac-V₁-L-T linkage. I haven't done much more about it, but we did find that K-12 itself (also 589161) is inhibited by leucine. In liquid minimal medium substantial inhibition is seen at 100 ug/ml, but was noticeable at less. As you noted, the inhibition is relieved by amino acids. I do not know whether this has any very direct bearing on L_m, except that we are probably running interquantitative modifiers, rather than a sharp segregation. Your interpretation of the origin of L_m seems more reasonable than ever. If we are dealing with an amino acid balance, it seems quite likely that an increased response to leucine qua growth factor would be accompanied by an increased sensitivity to it qua a.a. antagonist. Conceivably, it might be worth while to clarify this possibility in a footnote; Crow tells me this could be done. Otherwise, the whole matter may well be buried, which might be just as well also.

Some aspects of K-12 sex are very active again. We're collaborating with Cavalli on this. The enclosure gives part of the story. More recently it looks as if F+ x F+ crosses involve either a relative sexuality situation, or phenotypic variability in a so-called F+ culture. The whole T-L- line, starting from 679-680, is F-. The perturbed segregation behavior of filial T-L- stocks is a consequence of their being F+, which throws out this evidence for chromosomal aberration. The Mal-S elimination seems to be a regular feature, and its direction is likely determined by the polarity of the parents with respect to F. The segment from the F+ parent (relative or absolute) is the one which is cast out. I shouldn't be surprised if this segment is a whole chromosome or chromosome arm (if there is any residual structural heterozygosity, it amounts to the same thing), and the whole story looks more and more like *Sciara coprophila*. Hayes' experiments (Nature, Jan '52) fit in very well, though not those particular interpretations, which he seems to be revising drastically himself. Just now, I'm looking again at Cavalli's old Hfr strains, with very promising results.

Sincerely,

Joshua Lederberg

PS- 58-161